1

2 3

4

5

6

17

ខួ

10

1:

12

13

14

15

16

1.

## **CLAIM AMENDMENTS**

This listing of claims will replace all prior versions, and listings, of claims in the application.

## Listing of Claims:

(Currently amended) A method of protecting a tissue component in a subject in need thereof, comprising administering to the subject at least one pyrophosphate analog comprising the structure:

$$\begin{array}{c}
O \\
\parallel \\
-X - P - \begin{pmatrix}
O \\
\parallel \\
-X - P - \\
\downarrow \\
OH
\end{array} - X - R^{2}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$\underbrace{\times X'}_{\bullet} - \begin{pmatrix} OH \\ | \\ -P \\ | \\ OH \end{pmatrix}_{\bullet} = O$$

where  $\underline{n}$   $\underline{n}'=2-4$ ;  $\underline{X}$  is O; RCR<sup>1</sup>; CR; C ( $\underline{n}$   $\underline{n}'=4$ ), CH ( $\underline{n}$   $\underline{n}'=3$ ), or CH<sub>2</sub> ( $\underline{n}$   $\underline{n}'=2$ ); NH; N; S; and R and/or R<sup>1</sup> is H, OH, a small alkyl group, or (CH<sub>2</sub>)<sub>m</sub>NH<sub>2</sub> where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

17

ž

3

1

2

or a pharmaceutically acceptable salt thereof.

1 2.

(Original) The method of claim 1, wherein the tissue component is at least one of a receptor, a protein, a lipid, a nucleic acid, a carbohydrate, a hormone, a vitamin, and a cofactor.

3.

4.

(Original) The method of claim 2, in which the tissue component is a receptor for a neurotransmitter, a neuropeptide, a neurotrophin, a growth factor, a steroid, a histamine, a purine, a benzodiazepine, arachidonic acid, nitric oxide, carbon monoxide, an odorant, or an ion channel.

3

1

(Currently amended) A method of protecting tissue in a subject in need thereof from oxidative stress, comprising administering at least one pyrophosphate analog comprising

2

3 the structure:

4

.

5

v

13

9

10

11

$$\begin{array}{c}
O \\
\parallel \\
-X - P - \begin{pmatrix}
O \\
\parallel \\
-X - P - \\
\downarrow \\
OH
\end{array} - X - R^{2}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$\frac{X}{X'} - \begin{pmatrix} OH \\ | \\ -P = O \\ | \\ OH \end{pmatrix}_{\frac{1}{H}, \frac{1}{U}}$$

14

15 16

17

where n n'=2-4; X X' is O; RCR<sup>1</sup>; CR; C (n n'=4), CH (n n'=3), or CH<sub>2</sub> (n n'=2); NH; N;

S; and R and/or R<sup>1</sup> is H, OH, a small alkyl group, or (CH<sub>2</sub>)<sub>m</sub>NH<sub>2</sub> where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

5. (Withdrawn) A method of increasing the efficacy of an agent that directly or indirectly affects a receptor in a subject in need thereof, comprising administering the agent, and administering at least one pyrophosphate analog comprising the structure:

$$\begin{array}{c}
O \\
\downarrow \\
OH
\end{array} \left( \begin{array}{c}
O \\
\parallel \\
-X - P - \\
\downarrow \\
OH
\end{array} \right)_{n} - X - R^{2}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$X - \begin{pmatrix} OH \\ | \\ -P \\ OH \end{pmatrix}_{n}$$

where n=2-4; X is O; RCR<sup>1</sup>; CR; C (n=4), CH (n=3), or CH<sub>2</sub> (n=2); NH; N; S; and R and/or R<sup>1</sup> is H, OH, a small alkyl group, or  $(CH_2)_mNH_2$  where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

- 6. (Withdrawn) The method of claim 5, in which the receptor is a receptor for a neurotransmitter, a neuropeptide, a neurotrophin, a growth factor, a steroid, a histamine, a purine, a benzodiazepine, arachidonic acid, nitric oxide, carbon monoxide, an odorant, or an ion channel.
- 7. (Withdrawn) The method of claim 6, in which the receptor is one of muscarinic acetylcholine, nicotinic acetylcholine, an opiate, a catecholamine, serotonin, glutamate, aspartate, cannabinoid, gamma aminobutyric acid, or glycine.
- 8. (Withdrawn) The method of claim 6, in which the agent directly or indirectly affects a mAChR.
- 9. (Withdrawn) The method of claim 8, wherein the agent that directly or indirectly affects a mAChR comprises an anticholinesterase agent, a neurologic agent, or a muscarinic receptor agonist.
- 10. (Withdrawn) The method of claim 8, in which the agent that directly or indirectly affects a mAChR comprises Xanomeline.
- 11. (Withdrawn) The method of claim 8, wherein the agent that directly or indirectly affects a mAChR comprises donepezil, rivastigmine, galanthamine, metrifonate, or a combination thereof.

12. (Withdrawn) A method of protecting a subject from at least one carcinogenic metal, comprising administering to the subject at least one pyrophosphate analog comprising the structure:

$$R^{1}-X-P-\begin{pmatrix}O\\ \parallel\\-X-P-\\ \downarrow\\OH\end{pmatrix}_{D}-X-R^{2}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

$$X - \begin{pmatrix} OH \\ | \\ -P = O \\ | \\ OH \end{pmatrix}_{n}$$

or the structure:

where n=2-4; X is O; RCR<sup>1</sup>; CR; C (n=4), CH (n=3), or CH<sub>2</sub> (n=2); NH; N; S; and R and/or R<sup>1</sup> is H, OH, a small alkyl group, or  $(CH_2)_mNH_2$  where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

13. (Withdrawn) The method of claim 12, in which the carcinogenic metal is selected from the group consisting of arsenic, cadmium, cobalt, nickel, lead, and chromium.

14. (Withdrawn) A method of reducing poisoning of a subject by at least one metal, comprising administering to the subject at least one pyrophosphate analog comprising the structure:

$$\begin{array}{c}
O \\
\parallel \\
-X - P - \\
OH
\end{array}
\left(
\begin{array}{c}
O \\
\parallel \\
-X - P - \\
OH
\end{array}
\right) - X - R^{2}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$X - \begin{pmatrix} OH \\ | \\ -P = O \\ | \\ OH \end{pmatrix}_{n}$$

where n=2-4; X is O; RCR<sup>1</sup>; CR; C (n=4), CH (n=3), or CH<sub>2</sub> (n=2); NH; N; S; and R and/or  $R^1$  is H, OH, a small alkyl group, or  $(CH_2)_mNH_2$  where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

15. (Withdrawn) The method of claim 14, in which the metal is selected from the group consisting of iron, copper, mercury, lead, cadmium, vanadium and their alloys.

16.

(Withdrawn) A method of treating bacterial, fungal, algo, or algae infections in a subject in need thereof, comprising administering to the subject at least one pyrophosphate analog comprising the structure:

$$R^{1}-X-P - \begin{pmatrix} O \\ \parallel \\ -X-P - \\ | OH \end{pmatrix} -X-R^{2}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$X - \begin{pmatrix} OH \\ | \\ - P = O \\ | \\ OH \end{pmatrix}_n$$

where n=2-4; X is O; RCR $^1$ ; CR; C (n=4), CH (n=3), or CH $_2$  (n=2); NH; N; S; and R and/or R $^1$  is H, OH, a small alkyl group, or (CH $_2$ )<sub>m</sub>NH $_2$  where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

- 17. (Withdrawn) The method of claim 16, in which the subject is a plant.
- 18. (Withdrawn) The method of claim 17, in which the pyrophosphate analog comprises imidodiphosphate.

- 19. (Withdrawn) The method of claim 16, in which the subject is an animal or mammal.
- 20. (Withdrawn) A method of reducing toxic actions of metal ions in a subject in need thereof, comprising administering to the subject at least one pyrophosphate analog comprising the structure:

$$R^{1}-X-P-\begin{pmatrix}O\\ \parallel\\-X-P-\\0\end{pmatrix}-X-R^{2}$$

$$OH\begin{pmatrix}O\\ \parallel\\OH\end{pmatrix}_{n}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$X - \begin{pmatrix} OH \\ | \\ -P = O \\ | \\ OH \end{pmatrix}_{n}$$

where n=2-4; X is O; RCR<sup>1</sup>; CR; C (n=4), CH (n=3), or CH<sub>2</sub> (n=2); NH; N; S; and R and/or R<sup>1</sup> is H, OH, a small alkyl group, or (CH<sub>2</sub>)<sub>m</sub>NH<sub>2</sub> where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

21. (Withdrawn) The method of claim 20, in which the metal ion is selected from the group consisting of Fe<sup>++</sup>, Hg<sup>++</sup>, Cd<sup>++</sup>, Cu<sup>++</sup>, As<sup>+++</sup>, and Pb<sup>++</sup>.

22. (Withdrawn) A method of protecting a pharmacological agent in a formulation, comprising combining the agent with at least one pyrophosphate analog comprising the structure:

$$R^{1}-X-P - \begin{pmatrix} O \\ \parallel \\ -X-P - \\ | OH \end{pmatrix} -X-R^{2}$$

where each X is independently O, CH<sub>2</sub>, NH, or S; R<sup>1</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR<sup>2</sup>), or -(PO(OH)O)<sub>m</sub>-PO(OH)(OR<sup>2</sup>) and m is 1-3; R<sup>2</sup> is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$X - \begin{pmatrix} OH \\ -P \\ OH \end{pmatrix}_{n}$$

where n=2-4, X is O; RCR<sup>1</sup>; CR; C (n=4), CH (n=3), or CH<sub>2</sub> (n=2); NH; N; S; and R and/or  $R^1$  is H, OH, a small alkyl group, or  $(CH_2)_mNH_2$  where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

23. (Withdrawn) The method of claim 22, in which the pharmacological agent is a therapeutic agent.

- 24. (Withdrawn) The method of claim 22, in which the pharmacological agent is a diagnostic agent.
- 25. (Withdrawn) A method of increasing efficacy of a neurologic agent in a subject in need thereof, comprising administering to the subject the neurologic agent, and administering at least one pyrophosphate analog comprising the structure:

$$R^{1}-X-P - \begin{pmatrix} O \\ \parallel \\ -X-P - \\ | OH \end{pmatrix} - X-R^{2}$$

where each X is independently O,  $CH_2$ , NH, or S;  $R^1$  is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl,  $-PO(OH)(OR^2)$ , or  $-(PO(OH)O)_m-PO(OH)(OR^2)$  and m is 1-3;  $R^2$  is H, a small alkyl group, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and n is 1-900;

or the structure:

$$X - \begin{pmatrix} OH \\ | \\ -P = O \\ | \\ OH \end{pmatrix}_{D}$$

where n=2-4; X is O; RCR<sup>1</sup>; CR; C (n=4), CH (n=3), or CH<sub>2</sub> (n=2); NH; N; S; and R and/or R<sup>1</sup> is H, OH, a small alkyl group, or  $(CH_2)_mNH_2$  where m=1-6;

or a dinucleoside-5-5'-pyrophosphate, a cyclopyrophosphate of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate;

or a pharmaceutically acceptable salt thereof.

- 26. (Withdrawn) The method of claim 25, wherein the neurologic agent comprises a ganglioside, a phosphatidylserine, a nerve growth factor, a neurotrophin, a brain-derived neurotrophic factor, a fibroblast growth factor, an insulin, an insulin-like growth factor, a transforming growth factor, an epidermal growth factor, a platelet-derived growth factor, a neurokine, activity-dependent neurotrophic factor, a ciliary neurotrophic factor, a gliaderived neurotrophic factor, a gliaderived neurotrophic factor, a gliaderived nexin, a cholinergic enhancing factor, an antisense oligonucleotide, a DNA or RNA vector or plasmid that encodes one or more protein neurologic agents or nerve growth promoting factors, or a combination thereof.
- 27. (Withdrawn) The method of claim 26, wherein the ganglioside comprises GM-1 ganglioside.
- 28. (Withdrawn) The method of claim 26, wherein the neurotrophin comprises neurotrophin 3, neurotrophin 4, neurotrophin 5, or a combination thereof.
- 29. (Withdrawn) The method of claim 26, wherein the fibroblast growth factor comprises basic fibroblast growth factor, or acidic fibroblast growth factor.
- 30. (Withdrawn) The method of claim 26, wherein the insulin-like growth factor comprises insulin-like growth factor-I, insulin-like growth factor-2, or a combination thereof.
- 31. (Withdrawn) The method of claim 26, wherein the cholinergic enhancing factor comprises ethanolamine, thyroid hormone T.3, gallamine or a combination thereof.
- 32. (Currently amended) The method of any of claims 1, 4, 5, 12, 14, 16, 20, 22, or 25, wherein the pyrophosphate analog comprises pyrophosphate, imidodiphosphate, guanylimidodiphosphate, adenylylimidodiphosphate, tripolyphosphate, or a bisphosphonate.
- 33. (Original) The method of claim 32, wherein the pyrophosphate analog comprises etidronic acid, pamidronic acid, or a combination thereof.
- 34. (Original) The method of any of claims 1, 2, 5, 12, 14, 16, 20, 22, or 25, wherein the subject suffers from at least one of cancer; neuropathies, diseases, or disorders of the

heart, smooth muscles, blood, blood vessels, glands, or bones; hypertension; myocardial infarction, ischemic heart disease, or congestive heart failure; irritable bowel syndrome; diverticular disease; urinary incontinence; esophageal achalasia; chronic obstructive airways disease; cardiac arrhythmia; xerostomia; diabetes mellitus; Sjogren's syndrome; Paget's disease; hereditary hematochromatosis; or a non-CNS disorder resulting from normal aging.

- 35. (Original) The method of any of claims 1, 2, 5, 12, 14, 16, 20, 22, or 25, wherein the subject suffers from at least one of a neurologic disorder and a psychiatric disorder
- 36. (Original) The method of claim 35, wherein the subject suffers from at least one of Alzheimer's disease, Parkinson's disease, Lewy body dementia, multiple sclerosis, cerebellar ataxia, progressive supranuclear palsy, amyotrophic lateral sclerosis, an affective disorder, an anxiety disorder, schizophrenia, cell damage, nerve damage, a CNS infection, a tumor of the brain, a tumor of the spinal cord, a stroke in the brain, a stroke in the spinal cord, a prion disease, a CNS disorder resulting from ordinary aging, a brain injury, a spinal cord injury; or a non-CNS disorder resulting from normal aging.
- 37. (Original) The method of any of claims 1, 2, 5, 12, 14, 16, 20, 22, or 25, further comprising combining any pyrophosphate analog with at least one of a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- Original) The method of claim 37, further comprising administering heme oxygenase, a vector encoding a heme oxygenase-1, a vector encoding a heme oxygenase-1, heme oxygenase-2, a vector encoding a heme oxygenase-2, a biliverdin reductase, a vector encoding a biliverdin reductase, a vector encoding a catalase, a peroxidase, a vector encoding a peroxidase, or a combination thereof.
- 39. (Original) The method of claim 37, further comprising administering a heme binding protein.

- 40. (Original) The method of claim 39, wherein the heme binding protein comprises hemopexin, a lipoprotein, or a combination thereof.
- 41. (Original) The method of any of claims 1, 2, 5, 12, 14, 16, 20, 22, or 25, further comprising administering heme oxygenase, a vector encoding a heme oxygenase-1, heme oxygenase-2, a vector encoding a heme oxygenase-2, a biliverdin reductase, a vector encoding a biliverdin reductase, a catalase, a vector encoding a catalase, a peroxidase, a vector encoding a peroxidase, or a combination thereof.
- 42. (Original) The method of any of claims 1, 2, 5, 12, 14, 16, 20, 22, or 25, further comprising administering a heme binding protein.
- 43. (Original) The method of claim 42, wherein the heme binding protein comprises hemopexin, a lipoprotein, or a combination thereof.
- 44. (Original) The method of any of claims 1, 2, 5, 12, 14, 16, 20, 22, or 25, in which the compound is:

$$R^{1}-X- \begin{matrix} O & & & & \\ \parallel & & & \parallel \\ -X-P & - & & \parallel \\ -X-P & - & & \parallel \\ OH & OH \end{matrix} -X-R^{2}$$

and n is 1-6.

- (Withdrawn) A method of protecting a tissue component in a subject in need thereof, comprising administering to the subject a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- 46. (Withdrawn) The method of claim 45, wherein the tissue component is at least one of a receptor, a protein, a lipid, a nucleic acid, a carbohydrate, a hormone, a vitamin, and a cofactor.

- (Withdrawn) The method of claim 46, in which the tissue component is a receptor for a neurotransmitter, a neuropeptide, a neurotrophin, a growth factor, a steroid, a histamine, a purine, a benzodiazepine, arachidonic acid, nitric oxide, carbon monoxide, an odorant, or an ion channel.
- 48. (Withdrawn) A method of protecting tissue from oxidative stress, comprising administering a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- (Withdrawn) A method of increasing the efficacy of an agent that directly or indirectly affects a receptor in a subject in need thereof, comprising administering the agent, and administering a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- (Withdrawn) The method of claim 49, in which the receptor is a receptor for a neurotransmitter, a neuropeptide, a neurotrophin, a growth factor, a steroid, a histamine, a purine, a benzodiazepine, arachidonic acid, nitric oxide, carbon monoxide, an odorant, or an ion channel.
- 51. (Withdrawn) The method of claim 50, in which the receptor is one of muscarinic acetylcholine, nicotinic acetylcholine, an opiate, a catecholamine, serotonin, glutamate, aspartate, cannabinoid, gamma aminobutyric acid, or glycine.
- 52. (Withdrawn) The method of claim 49, in which the agent directly or indirectly affects a mAChR.
- (Withdrawn) The method of claim 52, wherein the agent that directly or indirectly affects a mAChR comprises an anticholinesterase agent, a neurologic agent, or a muscarinic receptor agonist.
- 54. (Withdrawn) The method of claim 52, in which the agent that directly or indirectly affects a mAChR comprises Xanomeline.

- (Withdrawn) The method of claim 52, wherein the agent that directly or indirectly affects a mAChR comprises donepezil, rivastigmine, galanthamine, metrifonate, or a combination thereof.
- (Withdrawn) A method of protecting a subject from at least one carcinogenic metal, comprising administering to the subject a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- 57. (Withdrawn) The method of claim 56, in which the carcinogenic metal is selected from the group consisting of arsenic, cadmium, cobalt, nickel, lead, and chromium.
- (Withdrawn) A method of reducing poisoning of a subject by at least one metal, comprising administering to the subject a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- 59. (Withdrawn) The method of claim 56, in which the metal is selected from the group consisting of iron, copper, mercury, lead, cadmium, and their alloys.
- 60. (Withdrawn) A method of treating bacterial, fungal, algo, or algae infections in a subject in need thereof, comprising administering to the subject a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- 61. (Withdrawn) The method of claim 60, in which the subject is a plant.
- 62. (Withdrawn) The method of claim 60, in which the subject is an animal or mammal.
- 63. (Withdrawn) A method of reducing toxic actions of metal ions in a subject in need thereof, comprising administering to the subject a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.

- 64. (Withdrawn) The method of claim 63, in which the metal ion is selected from the group consisting of Fe<sup>++</sup>, Hg<sup>++</sup>, Cd<sup>++</sup>, Cu<sup>++</sup>, As<sup>+++</sup>, and Pb<sup>++</sup>.
- 65. (Withdrawn) A method of protecting a pharmacological agent in a formulation, comprising combining the agent with at least one of a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- 66. (Withdrawn) The method of claim 65, in which the pharmacological agent is a therapeutic agent.
- 67. (Withdrawn) The method of claim 65, in which the pharmacological agent is a diagnostic agent.
- 68. (Withdrawn) A method of increasing efficacy of a neurologic agent in a subject in need thereof, comprising administering to the subject the neurologic agent, and administering a bilirubin, biliverdin, carnosol, quercetin, myricetin, a bioflavinoid, a combination thereof, or a pharmaceutically acceptable salt thereof.
- 69. (Withdrawn) The method of claim 68, wherein the neurologic agent comprises a ganglioside, a phosphatidylserine, a nerve growth factor, a neurotrophin, a brain-derived neurotrophic factor, a fibroblast growth factor, an insulin, an insulin-like growth factor, a transforming growth factor, an epidermal growth factor, a platelet-derived growth factor, a neurokine, activity-dependent neurotrophic factor, a ciliary neurotrophic factor, a gliaderived neurotrophic factor, a gliaderived neurotrophic factor, a gliaderived nexin, a cholinergic enhancing factor, an antisense oligonucleotide, a DNA or RNA vector or plasmid that encodes one or more protein neurologic agents or nerve growth promoting factors, or a combination thereof.
- 70. (Withdrawn) The method of claim 69, wherein the ganglioside comprises GM-1 ganglioside.
- 71. (Withdrawn) The method of claim 69, wherein the neurotrophin comprises neurotrophin 3, neurotrophin 4, neurotrophin 5, or a combination thereof.

- 72. (Withdrawn) The method of claim 69, wherein the fibroblast growth factor comprises basic fibroblast growth factor, or acidic fibroblast growth factor.
- 73. (Withdrawn) The method of claim 69, wherein the insulin-like growth factor comprises insulin-like growth factor-I, insulin-like growth factor-2, or a combination thereof.
- 74. (Withdrawn) The method of claim 69, wherein the cholinergic enhancing factor comprises ethanolamine, thyroid hormone T.3, gallamine or a combination thereof.
- (Withdrawn) The method of any of claims 45, 47, 48, 49, 56, 58, 60, 63, 65, or 68, wherein the subject suffers from at least one of cancer; neuropathies, diseases, or disorders of the heart, smooth muscles, blood, blood vessels, glands, or bones; hypertension; myocardial infarction, ischemic heart disease, or congestive heart failure; irritable bowel syndrome; diverticular disease; urinary incontinence; esophageal achalasia; chronic obstructive airways disease; cardiac arrhythmia; xerostomia; diabetes mellitus; Sjogren's syndrome; Paget's disease; hereditary hematochromatosis; or a non-CNS disorder resulting from normal aging.
- 76. (Withdrawn) The method of any of claims 45, 47, 48, 49, 56, 58, 60, 63, 65, or 68, wherein the subject suffers from at least one of a neurologic disorder and a psychiatric disorder.
- (Withdrawn) The method of claim 76, wherein the subject suffers from at least one of Alzheimer's disease, Parkinson's disease, Lewy body dementia, multiple sclerosis, cerebellar ataxia, progressive supranuclear palsy, amyotrophic lateral sclerosis, an affective disorder, an anxiety disorder, schizophrenia, cell damage, nerve damage, a CNS infection, a tumor of the brain, a tumor of the spinal cord, a stroke in the brain, a stroke in the spinal cord, a prion disease, a CNS disorder resulting from ordinary aging, a brain injury, a spinal cord injury, or a combination thereof.
- (Withdrawn) The method of any of claims 45, 47, 48, 49, 56, 58, 60, 63, 65, or 68, further comprising administering heme oxygenase, a vector encoding a heme oxygenase, heme oxygenase-1, a vector encoding a heme oxygenase-2, a vector

encoding a heme oxygenase-2, a biliverdin reductase, a vector encoding a biliverdin reductase, a catalase, a vector encoding a catalase, a peroxidase, a vector encoding a peroxidase, or a combination thereof.

- 79. (Withdrawn) The method of any of claims 45, 47, 48, 49, 56, 58, 60, 63, 65, or 68, further comprising administering a heme binding protein.
- 80. (Withdrawn) The method of claim 79, wherein the heme binding protein comprises hemopexin, a lipoprotein, or a combination thereof.